REMARKS

Claims 11, 19, 55, and 62-68 are currently pending in this application. Claims 1-10, 12-18, 20-54 and 56-61 were canceled without prejudice or disclaimer in prior amendments.

The amendment to claims 11, 19, and 55 is supported at page 77, lines 12-18. Claims 63, 65, and 67 are amended herein for grammatical reasons. No new matter is added by these amendments.

Supplemental Information Disclosure Statement

A Supplemental Information Disclosure Statement accompanies this response. Applicants respectfully request that the Examiner consider and make of record the publications contained therein, and return the initialed and signed Form PTO/SB/08.

Amendments to the Specification

The specification is amended to correct two statements regarding one of the figures. Panel B of Figure 23 indicates that the samples originate from human sera. The brief description of Figure 23 at page 11, line 33 to page 12, line 2 confirms that these samples are from sera. Additionally, page 43, lines 8-10; page 63, lines 15-18; page 64, lines 27-29; and page 99, lines 20-23 reiterate that the samples are serum samples. Accordingly, the statements on page 62 and on page 95 are corrected to reflect that the samples are serum samples, not whole tissue lysate samples. No new matter is added by these amendments.

Claim Objections

Claims 63, 65 and 67 have been amended to recite "by contacting the sample with an antibody or antibody fragment which is immunoreactive with said protein..." in order to render the claim grammatically correct. Withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 11, 19, and 55 were rejected under 35 U.S.C. § 112, second paragraph as not having sufficient antecedent basis for the limitation, "said 20P1F12/TMPRSS2 gene products."

Claims 11, 19, and 55 have been amended to recite "20P1F12/TMPRSS2 gene expression" instead of "said 20P1F12/TMPRSS2 gene products." The limitations as amended

have antecedent support in the respective claims. The Examiner's comment that the "independent claims clearly set forth that the 20P1F12/TMPRSS2 comprises SEQ ID NO:2" implies that the previous phrase "gene products," embraces only proteins. However, Applicants wish to note that 20P1F12/TMPRSS2 gene products and gene expression encompass both 20P1F12/TMPRSS2 mRNA and 20P1F12/TMPRSS2 protein. See, for example, page 59, lines 21 to 22 of the instant specification, which recites "the status of the 20P1F12/TMPRSS2 gene and gene products such as mRNAs and proteins."

Applicants submit that this amendment resolves any lack of antecedent basis, and respectfully request withdrawal of the rejection.

Claims 63, 65, and 67 were rejected under 35 U.S.C. § 112, second paragraph as vague for reciting "observing the presence or absence of an immunocomplex formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein." The Examiner indicated that is was not clear what was referred to by "any" 20P1F12/TMPRSS2 protein. While Applicants believe that the claims are clear as they stand, the word "any" has been struck from claims 63, 65, and 67. Applicants submit that this clarifies that the claim refers to the various forms of the 20P1F12/TMPRSS2 protein as described in the specification. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 11, 19, and 55 were rejected under 35 U.S.C. § 112, second paragraph as incomplete for omitting essential steps. The Examiner indicated that the claims omitted a measurement or contact step which implements the examination of the level of expression of the gene products.

This rejection is respectfully traversed. The person of skill in the art will know of many methods for examining the level of expression of gene products. In addition, the specification teaches a wide variety of methods for examining the level of expression of a gene, which include examining gene amplification by Southern blotting, Northern blotting, measurement of a DNA-RNA hybrid using an antibody (e.g., for detecting whether RNA is being transcribed on a DNA template), or measurement of a DNA-protein complex using an antibody (e.g., for detecting whether a transcription factor or an RNA polymerase has bound to DNA). These methods are discussed in the instant specification at page 73, line 30 to page 74, line 7; see also page 64, lines

4 to 11, which cites various chapters of Current Protocols in Molecular Biology that describe illustrative protocols.

In view of the level of skill in the art and the various methods of examining the level of expression of a gene taught in the specification, the Applicants believe that the recitation of "examining a level of expression of 20P1F12/TMPRSS2 gene" provides sufficient guidance to the person of skill in the art, such that an essential step has not been omitted. Applicants respectfully request withdrawal of this rejection.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 11, 19, 55, and 62-68 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. In particular, the Examiner indicated that one of skill in the art could not use or successfully practice the invention with any predictability.

This rejection is respectfully traversed. The Examiner stated that, "[i]f a molecule such as 20P1F12/TMPRSS2 is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the moleucle. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner." (Office Action mailed June 8, 2004, at page 5, first two sentences of first complete paragraph.) The specification clearly teaches expression patterns of 20P1F12/TMPRSS2 and related proteins (such as 20P1F12/TMPRSS2 cleavage products or complexes with other components) which differ between normal samples and prostate cancer samples.

For example, Figure 23 illustrates a clear difference in the expression of the 32 kD fragment of 20P1F12/TMPRSS2 between blood serum samples from normal males and prostate cancer patients. Normal sera has little to no expression of the 32 kD fragment, while sera from prostate cancer patients has higher expression of the 32 kD fragment. The left-hand-side gel of Panel B of Figure 23 illustrates 20P1F12/TMPRSS2 expression in blood serum from normal male, two colon cancer samples, and two prostate cancer samples, and in supernatant from cultured LNCaP prostate cancer cells. The right-hand-side gel of Panel B of Figure 23 illustrates 20P1F12/TMPRSS2 expression in blood serum from normal male and two prostate cancer samples. A comparison of the left-hand lanes of both gels in Panel B, which display samples from normal males, with the prostate cancer samples indicates that in two out of two normal

males, there is little to no expression of the 32 kD fragment, while in three out of four prostate cancer samples, the 32 kD fragment is expressed.

Therefore, the specification demonstrates an expression pattern that allows 20P1F12/TMPRSS2 to be used in a diagnostic manner to distinguish between normal samples and prostate cancer samples.

Applicants also note that other researchers have affirmed the potential of using 20P1F12/TMPRSS2 for detection and treatment of cancer, in articles published subsequent to the filing date of the instant application. The article by Vaarala *et al.*, "The TMPRSS2 gene encoding transmembrane serine protease is overexpressed in a majority of prostate cancer patients: detection of mutated TMPRSS2 form in a case of aggressive disease," Int. J. Cancer, 94(5):705-10 (2001), states that, in benign prostatic hyperplasia and prostate cancer tissue samples from 32 patients examined by *in situ* hybridization, "[e]xpression of TMPRSS2 gene was higher in cancer cells than that in benign cells in 84% of the specimens containing both benign and malignant tissues." This was determined by an analysis of mRNA transcript levels: "[i]n the prostate cancer specimens where both benign and cancer tissues were present, TMPRSS2 mRNA level (Table II) was higher in malignant areas than that in benign areas is 16 of 19 cases." (See Vaarala *et al.*, page 707, second column, third complete sentence.) The prepublication abstract by Wilson *et al.*, "The membrane-anchored serine protease, TMPRSS2, activates PAR-2 in prostate cancer cells," Biochemical Journal (2004), states that "TMPRSS2 is a type II transmembrane bound serine protease which has gained interest due to its highly localised expression to the prostate and its overexpression in neoplastic prostate epithelium." Independent researchers have thus confirmed that TMPRSS2 is overexpressed in cancerous states, and can be used as a marker for neoplastic prostate growth and prostate cancer. (The Varaala *et al.* article and Wilson *et al.* prepublication abstract are enclosed in the Supplemental Information Disclosure Statement which accompanies this response.)

Applicants note that the Examiner indicated in the Office Action mailed May 6, 2003, that claims 11 and 19 would be allowable if re-written in independent form. In view of this earlier indication and the comments above on the correlation between 20P1F12/TMPRSS2 and prostate cancer, Applicants respectfully request withdrawal of this rejection of claims 11, 19, 55, and 62-68.

CONCLUSION

Applicants submit that all outstanding objections and rejections have been addressed by this response. The Examiner is invited to call the undersigned agent if the Examiner believes that any issues can be resolved via a telephone conference.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582000820.

Respectfully submitted,

Dated: December 7, 2004 By: _____

Robert K. Cerpa
Registration No. 39,933

Morrison & Foerster LLP
755 Page Mill Road
Palo Alto, CA 94304-1018
Telephone 650-813-5715
Facsimile 650-494-0792